

Amendment to the Claims:

This listing of claims will replace all prior versions and listings of claims in the application.

Listing of Claims:

1. (Original) A method of treating or preventing a lung disease in a subject comprising, administering to the subject via a pulmonary, oropharyngeal, or nasopharyngeal route a compound comprising a therapeutic agent and a targeting element directed to a ligand, wherein the targeting element confers apical to basolateral transcytosis to the therapeutic agent in an *in vitro* transcytotic assay.
2. (Original) The method of claim 1, wherein the ligand is selected from the group consisting of pIgR, pIgR stalk, transferrin receptor, apo-transferrin, holo-transferrin, vitamin B12 receptor, FcRn, an integrin, Flt-1, Flk-1, Flt-4, a GPI-linked protein, a scavenger receptor, folate receptor, and low density lipoprotein receptor.
3. (Original) The method of claim 2, wherein the ligand is the pIgR stalk.
4. (Original) The method of claim 2, wherein the targeting element binds a non-secretory component region of pIgR.
5. (Original) The method of claim 1, wherein the therapeutic agent is a polypeptide or a nucleic acid.
6. (Original) The method of claim 5, wherein the therapeutic agent is an immune system modulator.
7. (Original) The method of claim 5, wherein the therapeutic agent is selected from the group consisting of an anti-tumor agent, an anti-infective agent, an anti-angiogenesis agent, and an apoptosis inducer.
8. (Original) The method of claim 5, wherein the therapeutic agent is selected from the group consisting of an enzyme, an interleukin, an interferon, a cytokine, a chemokine, TNF, taxol, an antibody, and combinations of any two or more thereof.

9. (Currently Amended) The method of claim 8, wherein the therapeutic agent is selected from the group consisting of IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-9, IL-12, IL-13, IL-15, interferon α , interferon β , interferon- γ , IP-10, I-TAC, MIG, α 1-antitrypsin, functional derivatives of any thereof, and combinations of any two or more thereof.

10. (Currently Amended) The method of claim 9, wherein the therapeutic agent is selected from the group consisting of IL-2, interferon α , interferon β , α 1-antitrypsin, and functional derivatives of any thereof.

11. (Original) The method of claim 1, wherein the compound is administered through inhalation.

12. (Original) A method according to claim 1, wherein the composition is administered in a form selected from the group consisting of liquid particles and solid particles.

13. (Original) A method according to claim 12, wherein the composition is administered as liquid particles having an average size of between about 1 μ m and about 20 μ m.

14. (Original) A method according to claim 13, wherein the composition is administered as liquid particles having an average size of between about 1 μ m and about 10 μ m.

15. (Original) The method of claim 1, wherein the compound, or a therapeutic portion thereof, is delivered into the lung with a pharmacokinetic profile that results in the delivery of an effective dose of the compound or a therapeutic portion thereof.

16. (Original) The method of claim 1, wherein at least 10% of the compound, or a therapeutic portion or metabolite thereof, administered to the subject undergoes apical to basolateral transcytosis from the pulmonary lumen.

17. (Original) The method of claim 15, wherein at least 20% of the compound, or a therapeutic portion or metabolite thereof, administered to the subject undergoes apical to basolateral transcytosis from the pulmonary lumen.

18. (Original) The method of claim 1, wherein the targeting element is selected from the group consisting of a polypeptide, a recombinant polypeptide, an antibody, an antibody fragment, a single-chain variable region fragment, a small molecule, an oligonucleotide, an oligosaccharide, a polysaccharide, a carbohydrate, a cyclic polypeptide, a peptidomimetic, and an aptamer.

19. (Original) The method of claim 1, wherein the lung disease is a primary tumor of the lung.

20. (Original) The method of claim 1, wherein the lung disease is a pulmonary metastasis from a primary tumor.

21. (Original) The method of claim 20, wherein the primary tumor is selected from the group consisting of a sarcoma, an adenocarcinoma, a choriocarcinoma, and a melanoma.

22. (Original) The method of claim 21, wherein the primary tumor is selected from the group consisting of a colon adenocarcinoma, a breast adenocarcinoma, an Ewing's sarcoma, an osteosarcoma and a renal cell carcinoma.

23. (Original) The method of claim 20, wherein the primary tumor is a renal cell carcinoma.

24. (Original) The method of claim 20, wherein the clinical presentation of the pulmonary metastasis is selected from the group consisting of a solitary metastasis, a cannonball, a lymphangitis carcinomatosa, and a pleural effusion.

25. (Original) The method of claim 1, wherein the lung disease is a respiratory tract infection.

26. (Original) The method of claim 1, wherein the lung disease is an infection of the lung.

27. (Original) The method of claim 1, wherein the lung disease is a bacterial infection.

28. (Original) The method of claim 27, wherein the bacterial infection causes tuberculosis.

29. (Original) The method of claim 1, wherein the lung disease is a viral infection.
30. (Original) The method of claim 29, wherein the viral infection causes severe acute respiratory syndrome (SARS).
31. (Original) The method of claim 1, wherein the lung disease is a fungal infection.
32. (Original) The method of claim 1, wherein the lung disease causes pneumonia.
33. (Original) The method of claim 1, wherein the lung disease is a disorder of the interstitium.
34. (Original) The method of claim 1, wherein the lung disease is a disorder of gas exchange or blood circulation.
35. (Original) The method of claim 1, wherein the lung disease is a disease of the airways.
36. (Original) The method of claim 1, wherein the lung disease is a disorder of the pleura.
37. (Original) The method of claim 1, wherein the lung disease is COPD.
38. (Original) The method of claim 1, wherein the lung disease is asthma.
39. (Original) The method of claim 1, further comprising administering to the subject a second therapeutic agent.
40. (Original) The method of claim 1, further comprising administering to the subject a vaccine directed against an infective agent.
41. (Original) The method of claim 1, further comprising administering to the subject a vaccine directed against a cancerous agent or a vaccine directed against a cancer-associated polypeptide.
42. (Previously Presented) The method of claim 2, wherein the targeting element binds to an epitope on pIgR or pIgR stalk that comprises an amino acid sequence selected from the group consisting of LRKED (SEQ ID NO: 37), QLFVNEE (SEQ ID NO: 38),

LNQLT (SEQ ID NO: 39), YWCKW (SEQ ID NO: 40), GWYWC (SEQ ID NO: 41),
STLVPL (SEQ ID NO: 42), SYRTD (SEQ ID NO: 43), QDPRLF (SEQ ID NO: 44) and
KRSSK (SEQ ID NO: 45).

43. (Previously Presented) The method of claim 2, wherein the targeting element
binds to pIgR or pIgR stalk in a region selected from the group consisting of:

- R1 From KRSSK (SEQ ID NO: 45) to the carboxy terminus of pIgR,
- R2a From SYRTD (SEQ ID NO: 43) to the carboxy terminus of pIgR,
- R2b From SYRTD (SEQ ID NO: 43) to KRSSK (SEQ ID NO: 45),
- R3a From STLVPL (SEQ ID NO: 42) to the carboxy terminus of pIgR,
- R3b From STLVPL (SEQ ID NO: 42) to KRSSK (SEQ ID NO: 45),
- R3c From STLVPL (SEQ ID NO: 42) to SYRTD (SEQ ID NO: 43),
- R4a From GWYWC (SEQ ID NO: 41) to the carboxy terminus of pIgR,
- R4b From GWYWC (SEQ ID NO: 41) to KRSSK (SEQ ID NO: 45),
- R4c From GWYWC (SEQ ID NO: 41) to SYRTD (SEQ ID NO: 43),
- R4d From GWYWC (SEQ ID NO: 41) to STLVPL (SEQ ID NO: 42),
- R5a From YWCKW (SEQ ID NO: 40) to the carboxy terminus of pIgR,
- R5b From YWCKW (SEQ ID NO: 40) to KRSSK (SEQ ID NO: 45),
- R5c From YWCKW (SEQ ID NO: 40) to SYRTD (SEQ ID NO: 43),
- R5d From YWCKW (SEQ ID NO: 40) to STLVPL (SEQ ID NO: 42),
- R5e From YWCKW (SEQ ID NO: 40) to GWYWC (SEQ ID NO: 41),
- R6a From LNQLT (SEQ ID NO: 39) to the carboxy terminus of pIgR,
- R6b From LNQLT (SEQ ID NO: 39) to KRSSK (SEQ ID NO: 45),

- R6c From LNQLT (SEQ ID NO: 39) to SYRTD (SEQ ID NO: 43),
- R6d From LNQLT (SEQ ID NO: 39) to STLVPL (SEQ ID NO: 42),
- R6e From LNQLT (SEQ ID NO: 39) to GWYWC (SEQ ID NO: 41),
- R6f From LNQLT (SEQ ID NO: 39) to YWCKW (SEQ ID NO: 40),
- R7a From QLFVNEE (SEQ ID NO: 38) to the carboxy terminus of pIgR,
- R7b From QLFVNEE (SEQ ID NO: 38) to KRSSK (SEQ ID NO: 45),
- R7c From QLFVNEE (SEQ ID NO: 38) to SYRTD (SEQ ID NO: 43),
- R7d From QLFVNEE (SEQ ID NO: 38) to STLVPL (SEQ ID NO: 42),
- R7e From QLFVNEE (SEQ ID NO: 38) to GWYWC (SEQ ID NO: 41),
- R7f From QLFVNEE (SEQ ID NO: 38) to YWCKW (SEQ ID NO: 40),
- R7g From QLFVNEE (SEQ ID NO: 38) to LNQLT (SEQ ID NO: 39),
- R8a From LRKED (SEQ ID NO: 37) to the carboxy terminus of pIgR,
- R8b From LRKED (SEQ ID NO: 37) to KRSSK (SEQ ID NO: 45),
- R8c From LRKED (SEQ ID NO: 37) to SYRTD (SEQ ID NO: 43),
- R8d From LRKED (SEQ ID NO: 37) to STLVPL (SEQ ID NO: 42),
- R8e From LRKED (SEQ ID NO: 37) to GWYWC (SEQ ID NO: 41),
- R8f From LRKED (SEQ ID NO: 37) to YWCKW (SEQ ID NO: 40),
- R8g From LRKED (SEQ ID NO: 37) to LNQLT (SEQ ID NO: 39), and
- R8h From LRKED (SEQ ID NO: 37) to QLFVNEE (SEQ ID NO: 38).

44. (Original) The method of claim 1, wherein the compound further comprises a PTD or MTS.

45. (Original) The method of claim 1, wherein the compound further comprises a second targeting element.

46. (Original) The method of claim 45, wherein the second targeting element is substantially identical to the first targeting element.

47. (Original) The method of claim 1, wherein the targeting element comprises two to four binding sites for the ligand.

48. (Original) The method of claim 47, wherein the targeting element is selected from the group consisting of an antibody, an Fab fragment, and a single chain variable region fragment (sFv) diabody.

49. (Original) The method of claim 1, wherein the targeting element comprises two to four single chain variable region fragments (sFv), each sFv comprising a heavy chain variable domain covalently linked, directly or through a polypeptide linker, to a light chain variable domain, wherein one or more of the sFvs is covalently or noncovalently associated with the therapeutic agent.

50. (Original) The method of claim 49, wherein at least one sFv binds to pIgR.

51. (Original) The method of claim 50, wherein at least one sFv binds to a non-secretory component region of pIgR.

52. (Original) The method of claim 50, wherein at least one sFv binds to pIgR stalk.

53. (New) The method of claim 1, wherein the therapeutic agent is α 1-antitrypsin.

54. (New) The method of claim 1, wherein the lung disease is emphysema.

55. (New) The method of claim 54, wherein the ligand is pIgR or pIgR stalk, the therapeutic agent is α 1-antitrypsin, and the targeting element is selected from the group consisting of antibody, a Fab fragment, and a single chain variable region fragment.

56. (New) The method of claim 30, wherein the ligand is pIgR or pIgR stalk, the therapeutic agent is α 1-antitrypsin, and the targeting element is selected from the group consisting of antibody, a Fab fragment, and a single chain variable region fragment.